Notice of Allowability	Application No.	Applicant(s)	
	08/477,097	LIVINGSTON ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed 10/21/2004*.

2. ☒ The allowed claim(s) is/are *100,106,107,109,110 and 112-125*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☒ to Paper No./Mail Date 6/10/1996
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *2/16/2005* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
02/22/2005

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with John White on February 16, 2005.

The application has been amended as follows:

In the claims:

100. (Currently Amended) A composition which comprises:

(a) a conjugate of (i) a derivative of a ganglioside, which ganglioside [(1)] is a GM2 or GD2 ganglioside and [(2)] comprises an unaltered sphingosine base, wherein the derivative differs from the ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the GM2 or GD2 ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ε- aminolysyl group of Keyhole Limpet Hemocyanin;

(b) QS-21; and

(c) a pharmaceutically acceptable carrier,

wherein the amount of the conjugated GM2 or GD2 ganglioside derivative is an amount between about 1 μg and about 200 μg, the amount of QS-21 is an amount between about 10 μg

and about 200 μg, the GM2 derivative or GD2 derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to GM2 [and] or GD2[, the] ganglioside[, the derivative of which is present in the conjugate].

112. (Currently Amended) A composition of claim 100 which comprises:

(a) a conjugate of (i) a derivative of a ganglioside, which ganglioside [(1)] is a GM2 or GD2 ganglioside and [(2)] comprises an unaltered sphingosine base, wherein the derivative differs from the ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the GM2 or GD2 ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ε- aminolysyl group of Keyhole Limpet Hemocyanin;

(b) QS-21; and

(c) a pharmaceutically acceptable carrier,

wherein the amount of the conjugated GM2 or GD2 ganglioside derivative is an amount between about 1 μg and about 200 μg, the amount of QS-21 is about 100 μg, the GM2 derivative or GD2 derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to GM2 [and] or GD2[, the] ganglioside[, the derivative of which is present in the conjugate].

114. (Currently Amended) A method of stimulating or enhancing production of an antibody directed to GM2 or GD2 in a subject which comprises administering to the subject an effective amount of a composition which comprises:

(a) a conjugate of (i) a derivative of a ganglioside, which ganglioside [(1)] is a GM2 or GD2 ganglioside and [(2)] comprises an unaltered sphingosine base, wherein the derivative differs from the ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the GM2 or GD2 ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ε- aminolysyl group of Keyhole Limpet Hemocyanin;

(b) QS-21; and

(c) a pharmaceutically acceptable carrier,

wherein the amount of the conjugated GM2 or GD2 ganglioside derivative is an amount between about 1 μg and about 200 μg, the amount of QS-21 is an amount between about 10 μg and about 200 μg, the GM2 derivative or GD2 derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to GM2 [and] or GD2[, the] ganglioside[, the derivative of which is present in the conjugate].

115. (Currently Amended) A method of treating a human subject having a cancer which comprises administering to the subject an effective cancer-treating amount of a composition which comprises:

(a) a conjugate of (i) a derivative of a ganglioside, which ganglioside [(1)] is a GM2 or GD2 ganglioside and [(2)] comprises an unaltered sphingosine base, wherein the derivative differs from the ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the GM2 or GD2 ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ε- aminolysyl group of Keyhole Limpet Hemocyanin;

(b) QS-21; and

(c) a pharmaceutically acceptable carrier,

wherein the amount of the conjugated GM2 or GD2 ganglioside derivative is an amount between about l μg and about 200 μg, the amount of QS-21 is an amount between about 10 μg and about 200 μg, the GM2 derivative or GD2 derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to GM2 [and] or GD2[, the] ganglioside[, the derivative of which is present in the conjugate].

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: the rejections under 35 U.S.C. 103(a) are withdrawn in view of applicants' persuasive arguments that one of ordinary skill in the art would not have had a reasonable expectation of success in using QS-21 to increase the immunogenicity of a ganglioside conjugate in view of the teachings of Marciani, which are directed to using QS-21 to increase the immunogenicity of a viral peptide antigen. The rejection

under 35 U.S.C. 112, 2nd paragraph is withdrawn in view of the amendment to the claims and to the specification, and the statements made on record by applicants' representative that the amendatory material from the Kensil reference and the Newman reference consist of the same material incorporated by reference in the referencing application and the specification as amended does not raise any issue of new matter. The rejection under 35 U.S.C. 112, first paragraph is withdrawn in view of the amendment to the claims.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

alh

Anne L. Holleran
Patent Examiner
February 17, 2005

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
02/22/2005